

# Prospective single-center observational study of a new dietary supplement containing collagens type I, II, V, and X

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## Abstract

**Introduction:** The present prospective single-center observational study investigated the safety and efficacy of TendoGuard, a new dietary supplement containing collagen type I, II, V, and X.

**Methods and materials:** A goniometer was used to measure the range of motion, a pain scale (Borg) was applied to subjectively percept the pain, and a properly calibrated sphygmomanometer was utilized to evaluate muscle strength.

**Results:** The results indicated that administration of 750 mg/day of TendoGuard for 60 days improved essential symptoms in individuals suffering from joint diseases, including range of motion, general pain, and muscle strength. No adverse effects were detected during the observation period.

**Conclusion:** The results support the view that TendoGuard may be administered to patients suffering from joint diseases. These data encourage its use for patients suffering from degenerative joint diseases, including cartilage injuries, connective tissue disorders, polychondritis, joint defects, osteoarthritis, and rheumatoid arthritis.

**Key words:** Collagen, Joint Diseases, Range of Motion, General Pain, Muscle Strength.

## Introduction

TendoGuard, an association of collagens type I, II, V, and X, is a dietary supplement that may be beneficial for patients suffering from degenerative joint diseases, including cartilage injuries, connective tissue disorders, polychondritis, joint defects, osteoarthritis, and rheumatoid arthritis. Its use in the treatment of degenerative joint diseases has in-

creasingly gained support in medical community, and among consumers<sup>(1)</sup>.

It has been verified, in preclinical studies, that orally administered collagen is thoroughly absorbed by the intestine and circulated in the blood stream, remaining in the gastrointestinal tract. It was also revealed that a significant amount of collagen hydrolysate-derived peptides reaches cartilage tissue<sup>(2)</sup>. Additionally, it was exposed that treatment of cultured chondrocytes induced a statistically significant dose-dependent increase in collagen synthesis of the chondrocytes in cell culture experiments<sup>(3)</sup>.

Hyaline articular cartilage is a highly specialized avascular tissue that covers the surface of the diarthrodial joints, consisting of 5% of cells, the chondrocytes, which are immersed in the extracellular matrix. These cells present in small proportions are considered the metabolic center and producer of the vast extracellular matrix found in cartilage, composed basically of water, proteoglycans, collagen and other proteins. Water accounts for about 65-85% of the dry weight of the fabric, while the major macromolecules, such as collagen and proteoglycans, account for about 10% to 30% of the dry weight of the fabric, respectively<sup>(4)</sup>.

The composition and complex structural organization between collagen and proteoglycans ensures the inherent properties of articular cartilage, such as strength, elasticity and compressibility, necessary to dissipate and cushion the forces, as well as reduce friction, to which the diarthrodial joints are subjected, without much energy expenditure. Therefore, the integrity of the articular cartilage components is essential to ensure normal joint function<sup>(5)</sup>.

Collagen is the main structural element that confers tissue resistance; it is known that in addi-

tion to the support function, it participates in cell differentiation, adhesion, migration and proliferation, also exerting antigenic activity<sup>(5,6)</sup>.

The articular cartilage is composed primarily of collagen type II, with at least ten additional collagens, including types III, VI, IX, X, XI and XIII, present as minor constituents<sup>(7, 8, 9)</sup>. Of these, types II, VI, IX and XI were identified in cartilage in amounts sufficient to be isolated from tissue or from chondrocyte culture<sup>(10)</sup>.

Type V collagen is proportionally the smallest mass component in tissues but plays a key role in tissue proliferation and repair processes. Its presence in the basement membrane of vessels and in some mesenchymal tissues is of extreme importance in the connection between collagen IV of the basement membrane and the loose connective organ, actively participating in the interaction of extracellular matrix components and establishing association with other types collagen<sup>(11)</sup>.

Except for collagen type X, these collagens are also found in structures similar to cartilage, such as vitreous humor of the eye, developing cornea, nucleus pulposus discus and intra-articular meniscus. Recent studies have shown that the organization of collagen molecules in the vitreous and cartilage fibrils is identical<sup>(12)</sup>.

Collagen type X, also cartilage-specific, is a homotrimer, considerably shorter than type II and XI collagens. Type X has helical and non-helical domains, in addition to a large non-helical carboxy-terminal domain. This collagen is more abundant in hypertrophic cartilage, in the transition between cartilage and bone<sup>(13)</sup>.

Based on the findings that collagen is absorbed in its molecular form, accumulating in cartilage, and is able to stimulate chondrocyte metabolism<sup>(14)</sup>, it might be reasonable to use the association of collagens type I, II, V, and X, as a nutritional supplement to activate collagen biosynthesis in chondrocytes in humans, especially patients suffering from degenerative joint diseases. Thus, the aim of this single-center investigation is to extend these earlier findings with TendoGuard.

## Methods and materials

In accordance with the ethical standards of the Ethics Committee of Mortec Scientific, Inc. (Cam-

bridge, ON, Canada) on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000 and 2008, this prospective single-center clinical observational study was approved by its responsible committee, and managed in its Department of Clinical Medicine. According to study schedule, the consent form was discussed, signed, and a complete physical examination was executed at screening. Activity level, diet history, medication/supplement use and medical history were recorded.

Subjects' complaints of joint discomfort were recorded using pre- and post-treatment questionnaires to evidence personal data and issues related to an individual's functional quality. A goniometer was used to measure the range of motion<sup>(15)</sup>, a pain scale (Borg) was applied to subjectively percept the pain<sup>(16)</sup>, and a properly calibrated sphygmomanometer was utilized to evaluate muscle strength<sup>(17)</sup>.

Urine was collected for a pregnancy test for women of childbearing potential. A blood sample was taken for determination of alanine transaminase (ALT), aspartate transaminase (AST), bilirubin, blood urea nitrogen (BUN) and creatinine. Upon review of blood test results, eligible subjects were instructed to get an X-ray of the affected joints to confirm diagnosis. A total of 20 subjects were recruited using the inclusion and exclusion criteria outlined in Table 1.

At the first visit, selected subjects, properly informed by the Consent Term approved by the Scientific Committee of the Institute, were assigned to receive 750 mg of TendoGuard™ (Certified Nutraceuticals, Inc., San Diego, CA) daily. At the final visit, subjects were required to come to the clinical division for clinical assessment. A subject treatment diary was completed by each patient throughout the study period to determine product compliance, side effects, and supplementation use.

By GraphPad InStat 3.1, the Wilcoxon's test was used to compare non-parametric variables, whereas the variance analysis (ANOVA) test was used for parametric ones. A significance level of 5% was adopted in all comparisons and statistically significant results were marked with an asterisk (\*).

Table 1. Inclusion and exclusion criteria

Inclusion criteria
Males and females 45-75 years old
Females of childbearing potential must agree to use a medically approved form of birth control and have a negative urine pregnant test result
Disorder of the knee for more than three months
Able to walk
Availability for duration of study
Subject agrees not to start any new therapies during the course of the study
Able to give informed consent
Exclusion criteria
History of asthma, history of diabetes
Hyperuricemia
Hypersensitivity to NSAIDs
Abnormal liver or kidney function tests
Abnormal findings on complete blood count
Uncontrolled hypertension
History of allergic reaction to any ingredients in the test product
Hyperkalemia (potassium > 6.2 mmol/L)
History of cancer as well as gastrointestinal, renal, hepatic, cardiovascular, hematological, or neurological disorders
Anticipated problems with product consumption
High alcohol intake (>2 standard drinks per day)
History of psychiatric disorder that may impair the ability of subjects to provide written informed consent
Use of concomitant prohibited medication (narcotics, NSAIDs)
Any other condition that, in the opinion of the investigator, would adversely affect the subject's ability to complete the study or its measures

**Results**

Baseline characteristics of patients are summarized in Table 2. Where applicable, values are expressed as mean ± standard deviation.

Table 2. Baseline characteristics of patients.

Characteristics of patients	Values
Age (years)	55.9 ± 7.91
Sex (male/female)	10/10
Height (cm)	168.1 ± 8.52
Weight (kg)	81.3 ± 14.6
Systolic blood pressure (mm)	120.5 ± 7.84
Diastolic blood pressure (mm)	80.6 ± 8.33
Heart rate (bpm)	68.9 ± 7.42

The results are presented in Table 3 and Table 4 listing values for average, and standard deviation for each analyzed variable. Statistically significant results are marked with an asterisk (\*)

Table 4. Pre- and post- treatment groups.

Comparison	P
Range of motion	0,011*
General pain	0,001*
Muscle strength	0,004*

These results indicate that administration of 750 mg/day of TendoGuard for 60 days improved essential symptoms in individuals suffering from joint diseases, including range of motion, general pain,

Table 3. Range of motion, pain and muscle strength.

Treatment	Range of motion <sup>15</sup>		General pain <sup>16</sup>		Muscle strength <sup>17</sup>	
	Pre	Post	Pre	Post	Pre	Post
Average	105,22	172,53	8,73	1,92	58,43	104,97
Standard deviation	13,46	10,81	10,54	12,73	10,54	11,73
Standard error	4,22	4,93	4,76	5,48	4,76	5,68

and muscle strength. No adverse effects occurred during the 60-day observation period. The treatment was reported to be well tolerated by subjects.

### Discussion and conclusion

Several nutritional supplements, including chondroitin, glucosamine, soybean unsaponifiables and diacerein have emerged as new treatment options for joint disorders in the last few years<sup>(18)</sup>. The aim of this prospective single-center investigation is to evaluate the safety and the efficacy of a new dietary supplement containing collagens type I, II, V, and X, TendoGuard, which is a complex structural protein that may provide strength and flexibility to connective tissues.

It was investigated, in an observational study, the use of collagen hydrolysate as a nutritional supplement to reduce symptoms of joint damage, with the expectation that this change would reflect improvements in joint health. Individuals were recruited who had not been diagnosed with degenerative joint disease but who complained about joint pain that both the treating physician and the subjects interpreted as being a result of stressful exercising. It was reported that 78% of individuals at the end of the study noticed substantial improvement of their joint symptoms, including range of motion, pain, and muscle strength<sup>(19)</sup>.

The evaluation of muscle strength is an important technique to diagnose the etiology of the disease, and to define rehabilitation strategies. The muscle weakness, which was observed in our study during the pre-treatment assessments, is directly associated with knee joint pain and joint disability<sup>(20)</sup>.

Osteoarthritis results in changes that affect not only intracapsular tissue, as well as periarticular tissues, such as ligaments, capsules, tendons and muscles. Osteoarthritis patients compared to healthy individuals of the same age had muscle weakness, reduced knee proprioception, reduced balance and position sense<sup>(21)</sup>.

The presence of joint effusion, even in small amounts, is a potent inhibitory mechanism reflex muscular activity of the joints. A reduced reflex muscular activity causes hypotrophy and weakness early, with the resultant associated mechanical damages, such as decreased range of motion<sup>(22)</sup>.

Muscle strength declines rapidly during the detention of a member by decreasing the size of the muscle and stress per unit of the muscle cross-sectional area. The largest absolute loss of muscle mass occurs at the beginning of hypotrophy process. The pain inhibits reflex muscular activity, causing atrophy, and muscle weakness<sup>(23)</sup>.

The purpose of this study was to define whether administration of 750 mg of TendoGuard daily would reduce joint pain in patients suffering from joint diseases. The design of the observational study was appropriate to reveal that collagens type I, II, V, and X as a nutritional supplement ingested over 60 days was safe and efficacious in reducing symptoms of joint discomfort. The results of the study provide data supporting the view that TendoGuard may be administered to patients suffering from joint diseases. Further research will elucidate additional benefits from this association of collagens type I, II, V, and X.

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